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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GOLDBERG, JEANINE ANNE	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/039,288	BASTIAN, BORIS C.	
	Examin r	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *903* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed September 11, 2003. Currently, claims 1-20 are pending. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

2. Any objections and rejections not reiterated below are hereby withdrawn.

New Grounds of Rejection Necessitated by Amendment

New Matter

3. Claims 19-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the amended claims, reference to "detecting no chromosomal structural aberrations and at least one numerical aberration in chromosome, wherein the numerical aberration does not comprise a loss of whole chromosome 9 or a loss of whole chromosome 10" are included. The amendment proposes that the new claim language is supported on page 21 and 23. The specification, on page 21, teaches that the predominant pattern in the cases of group IV was gain or loss of entire chromosomes only. This differs from the aberration pattern observed in melanoma in which most cases have aberrations involving only partial chromosomes (page 21). However, the specification does not describe or discuss "detecting no chromosomal structural aberrations and at least one numerical aberration in chromosome, wherein

the numerical aberration does not comprise a loss of whole chromosome 9 or a loss of whole chromosome 10". The concept of "detecting no chromosomal structural aberrations and at least one numerical aberration in chromosome, wherein the numerical aberration does not comprise a loss of whole chromosome 9 or a loss of whole chromosome 10" does not appear to be part of the originally filed invention. Therefore, "detecting no chromosomal structural aberrations and at least one numerical aberration in chromosome, wherein the numerical aberration does not comprise a loss of whole chromosome 9 or a loss of whole chromosome 10" constitutes new matter. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3, 5-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for typing a skin tumor sample as a congenital melanocytic nevus by detecting the loss of complete chromosome 7, does not reasonably provide enablement for detecting whole chromosome loss or gain and detecting a gain of chromosome 10 or 11 alone or absence of loss at chromosome 9 or 10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn to a method of typing a growth arising in association with a congenital melanocytic nevus by analyzing chromosomal changes selected from the group consisting of gain of chromosome 10, gain of chromosome 11, a loss of chromosome 7 or a combination thereof, thereby typing the skin tumor sample as a benign growth.

The art teaches chromosomal analysis for Spitz nevi, melanoma, superficial spreading melanoma (SSM) and acral lentiginous melanoma (AM). Bastian et al (US Pat. 6,261,775, July 17, 2001) teaches CGH analysis of primary cutaneous melanomas and Spitz nevi (Figures 1 and 2). As seen in Figure 1, primary cutaneous melanomas lack a loss of chromosome 7, a gain in chromosome 10 and have partial gains in chromosome 11. As seen in Spitz nevi (Figure 2), partial chromosomal gains are seen in chromosome 11.

Bastian (US Pat. 6,465,180, October 15, 2002) illustrates chromosomal localizations of DNA sequence copy number changes in AM and SSMs detected by

CGH. As seen in Figure 1, chromosome 7 is not lost, chromosome 10 is not gained, however chromosome 11 contains gains in partial regions.

Thompson et al (Cancer Genet. Cytogenet. Vol. 83, pages 93-104 1995) teaches the analysis of melanoma. As seen in Figure 2, the chromosome profiles from 49 cases were analyzed. It is apparent that melanoma contains partial losses in chromosome 7 are present, partial gains in chromosome 10 and 11 are present.

Bastian et al. (Cancer Research, Vol. 58, pages 2170-2175, May 1998) teaches chromosomal gains and losses in melanomas. In approximately 50% of melanomas, chromosome 7 was gained. Additionally, 8 was gained in 34%, chromosome 20, 17, 2 was gained in 13%. It is apparent that melanoma contains gains of entire chromosomes, such that typing of a nodule as benign would be unpredictable.

The specification teaches performing comparative genomic hybridization on congenital melanocytic nevus. Table 2 teaches the frequency of observed changes. Based upon the Table, the following changes were observed

	CMN from Table 2	Primary cutaneous melanoma from Table 3
Gain of Chromosome 10	1/10	
Gain of Chromosome 11	1/10	
Loss of Chromosome 7	3/10	0/122

The specification also teaches 20% of proliferative nodules in CMN comprise a loss of whole chromosome 9 or 10. Thus, a method of typing a congenital melanocytic nevus as benign would be unpredictable. Loss of entire chromosome 9 and 10 occur in several CMN nodules, such that identification and typing based upon the lack of absence would be unpredictable (see Table 3, page 27).

Neither the art nor the specification teaches how to use the claimed invention as broadly as claimed.

The data in the specification teaches that the gain of chromosome 10 and 11 in a single CMN sample. The specification fails to provide any examples indicating that merely a gain in chromosome 10 or merely a gain in chromosome 11 has been found in any CMN. Moreover, the presence of a single sample is not a trend. No reasonable artisan would infer a method of typing a growth as a CMN by the detection in a single sample. The specification does not indicate that the finding of this single sample demonstrates that the association between the gain in chromosomes 10 and 11 and congenital melanocytic nevus. A representative number of samples were not analyzed which showed a correlation between gain of chromosome 10 or 11 and the occurrence in CMN. The specification does not provide any statistical analysis that demonstrates that this isolated occurrence is a reliable means for typing a growth arising in association with a congenital melanocytic nevus. Therefore, the skilled artisan would be required to perform additional undue experimentation to determine whether this chromosomal change is in fact associated with congenital melanocytic nevus or whether this chromosomal change is merely an outlier and an anomaly. Moreover, based upon

the data presented in the specification it is unpredictable that a detection of a gain of chromosome 10 or gain of chromosome 11 alone is predictably associated with congenital melanocytic nevus. The specification only demonstrates a congenital melanocytic nevus which contains both of these gains in additional gains in chromosomes 16, 20 and 22. Since the underlying principles of congenital melanocytic nevus have not been established, the skilled artisan would be unable to evaluate whether a gain of chromosome 10 or 11 alone would predictably type a skin tumor sample as a congenital melanocytic nevus. While one could conduct additional experimentation to determine whether the gain of the entire chromosome 11 or 10 might be associated with congenital melanocytic nevus, the outcome of such research cannot be predicted, and such further research and experimentation are both unpredictable and undue.

With respect to absence of loss of chromosome 9 or 10 as indicative of a benign growth, the specification teaches several incidences of loss of 9 and 10 in benign nodules. The art teaches that gains in various copy numbers in melanoma cells is detected. In approximately 50% of melanomas, chromosome 7 was gained. Additionally, 8 was gained in 34%, chromosome 20, 17, 2 was gained in 13%. It is apparent that melanoma contains gains of entire chromosomes, such that typing of a nodule as benign would be unpredictable. Claim 19, as written requires the detection of no chromosomal structural aberrations and at least one numerical aberration in chromosome. The specification does not support the no chromosomal structural aberrations. As seen in Case D168 and CN31, each of these individuals has a loss of

chromosome 9, but also has a structural aberration. Moreover, as taught in the instant specification, losses of whole chromosomes 9 and 10 are present in 20% of the nodules. Thus, a method of typing a nodule as benign based on the absence of loss of whole chromosome 9 or 10 is unpredictable.

Response to Arguments

The response traverses the rejection. The response asserts that the comparison of the loss or gain of chromosomes to congenital nevi cases and 108 melanomas is significant. The response asserts that while only one sample exhibited the claimed gain of whole chromosome 10 and 11, the fact that the changes were not observed in any of the melanoma samples is significant. This argument has been reviewed but is not convincing because it is unpredictable that the single sample in which a gain of 10 and 11 were found was not due to the combination, due to the presence of 16, 20, 22 and loss of 12. There were significant changes in the sample and it is unpredictable that the combination did not give rise to the significance, a subcombination is not indicative of benign growth or further whether the loss of chromosome 10 or 11 alone was indicative of benign growth. For example, gain of chromosome 20 appears to be found in two of the samples, however, there is no assertion that this chromosome alone is indicative of benign growth, as it is also found in 13% of melanomas (see Bastian et al. Cancer Research, Vol. 58, 1998). The skilled artisan would not have reasonably expect the gain of whole chromosome 10 or 11 as indicative of a benign growth because the single sample containing a gain of 10 or 11 contains gains and losses of entire chromosome 10, 11, 16, 20, 22 and 12. Thus, the skilled artisan would unlikely determine that either

gain or 10 or 11 alone would be indicative of benign. The skilled artisan would require further research to determine whether gain of 10 or 11 alone in additional benign samples was a trend or whether the specific sample illustrated in the specification was an anomaly in which the aggregate of chromosomal losses and gains resulted in the benign status of the nodule.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 20 are indefinite over the recitation "a gain or loss of a whole chromosome selected from 3-5, 7-12, 15-16, 20-22." Claim 19 appears to exclude loss of whole chromosome 9 or 10 from the possible aberrations. Claim 20 appears to include losses of whole chromosome 9 and 10. Thus, it is unclear whether Claim 20 is intended to further limit 20 or whether there is an alternative meaning to the claim.

Allowable Subject Matter

6. Claim 4 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claim 4 is directed to a method of typing a proliferative nodule as benign by detecting a loss of chromosome 7. The specification illustrates that 3/10 (30%) proliferative nodules in CMN as compared to 0% of primary melanomas contains a loss of whole chromosome 7. The art neither teaches nor suggests a loss of entire chromosome 7 is indicative of benign growth as opposed to melanoma. Thus, the limitations of Claim 4 are free of the art and supported by the specification.

Conclusion

7. No claims allowable.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Goldberg
October 29, 2003

Jehanne Souaya
JEHANNE SOUAYA
PATENT EXAMINER
10/29/03